

ANTON DE HAEN, LOUIS ODIER, AND THE INOCULATION CONTROVERSY

An editorial published in the *Bulletin of the New York Academy of Medicine* in July 1972¹ described a 17th century map of Geneva in which two hospitals were portrayed—the Hôpital Général and the Hôpital des Pestiférés. Mention of the latter establishment brought to mind Louis Odier (1748-1817), a Genevan physician eminent because of his work on infectious diseases. It is interesting and instructive to review a controversy in which Odier participated.

In the year 1757 Anton de Haen, the notoriously irascible professor of medicine in Vienna, published his *Questions on the Inoculation of Smallpox*,² in which he solicited replies from the learned. In 1759 he published a diatribe against inoculation.³

To the contentions of de Haen, Odier replied in a series of four letters published in the *Journal de Médecine, Chirurgie, Pharmacie, &c.*,⁴ during a period of four years. His observations and comments merit careful examination, since they give insight into 18th century concepts of communicable disease and into 18th century statistical methods.

Odier opens his first letter by remarking, in typical 18th century style, that although he did not have the honor of being personally acquainted with de Haen, he took the liberty of transmitting in an open letter some recent original observations on mortality from smallpox. De Haen had been the first to assert that inoculation had done more harm than good. He had submitted impressive proofs, which called for review.

Further, he had invited discussion. Accordingly Odier proposed to ascertain whether it is true, as de Haen had written, that mortality from smallpox had increased greatly in London since inoculation was introduced. Next he would attempt to discover whether the alleged change

1. Jarcho, S.: Hospitals depicted in old maps and panoramas (IV): Seventeenth century Geneva. *Bull. N.Y. Acad. Med.* 48:880-83, 1972.

2. Haen, Antonius de: *Quaestiones Saepius Motae Super Methodo Inoculandi Variolas, Ad Quas Directa Eruditorum Responsa Hucusque Desiderantur*. Vienna, Trattner, 1757. 80 pp.

3. Haen, Antonius de: *Réfutation de l'Inoculation*. Vienna, Trattner, 1759. 11 + 143 pp. For an ample study of the inoculation controversy see Klebs, A. C.: The historic evolution of variolation. *Bull. Johns Hopkins Hosp.* 24:69-83, 1913.

4. Odier, L.: *J. de Méd. Chir. Pharm.* 40:237-56, 1773; 40:331-52, 1773; 45:24-45, 1776; 47:298-315, 1777.

dated from the inception of inoculation. Finally he would attempt to develop a verdict for or against inoculation.

Odier had obtained all the London mortality reports (*extraits-mortuaires*) for the 112 years from 1661 to 1772 inclusive. In order to compensate for variations in the size of the total population and for errors in reporting, he derived for each year the ratio between the number of reported smallpox deaths and the total number of reported deaths. From the crude total of deaths from all causes he previously subtracted a special anomalous component, the deaths from plague, which distorted the figures for 1661-1680.

Additional difficulty was caused by the fact that in the reports for 1687-1700 measles was confounded or combined with smallpox. The size of the requisite correction had been debated in the medical press. Odier averaged the measles deaths reported during the 16 years which preceded and followed the period of confusion. He thereby derived the figure of 114 inferred measles deaths during each of the 14 confused years.

For years subsequent to 1700 the London statistics were further complicated by the inclusion of a puzzling entity called *Flox* [flux?]. Its nature was utterly obscure. Odier concluded that it was probably a kind of smallpox (*ce n'étoit probablement qu'une variété de la vérole volante*), infrequently fatal and statistically insignificant.

Odier's table shows the deaths from smallpox in London for every year from 1661 to 1772; a caesura between 1716 and 1717 marks the start of inoculation. The four columns of the tabulation show respectively the year, the number of baptisms, the number of burials, and the number of deaths from smallpox.

If inoculation is truly useful, says Odier, the mortality reports should reveal a decline in smallpox mortality during the years in which the procedure has been employed. The tables show that during the 56 years which preceded the start of inoculation smallpox had caused 1/16 of all deaths; in the subsequent 56 years it had caused more than 1/11. This rise in mortality produced a calculated excess of 35,129 deaths in London alone and perhaps 300,000 in the entire kingdom. The increase should not be attributed to inoculation, since it may have been due to other factors, which Odier reserved for discussion in the next installment.

Odier opens his second letter by discussing some differences between

his statistics and those of other writers, especially one Relhan of London. Odier feels that his own figures are the more reliable, since they are based on the weekly reports, whereas other physicians had used the less exact annual compilations. While it is true that smallpox mortality had increased since inoculation, it is by no means certain that the increase *began* when inoculation was introduced.

In order to throw light on this question Odier divided the 56 years between 1661 and 1716 into eight consecutive seven-year periods. This might reveal whether the outbreaks showed any regularity in their times or their vigor. Odier found that in the postinoculation era smallpox increased; instead of causing 1/11 of deaths in London it had reached a level of 1/9. He felt that the increase must be dated from the time that inoculation was introduced and that the increase apparently corresponded with the spread of inoculation. He noted however that the early popularity of inoculation was almost extinct by 1743; after this it was revived.

At this point Odier offers an interesting critique of the available statistics. It might be true, he says, that the tables were inexact in detail because of negligence and ignorance but to some extent these pitfalls were avoided by the use of ratios instead of absolute figures. Moreover, English physicians had assured Odier that, whatever the inaccuracies, smallpox deaths were reported more reliably than deaths from any other cause. Further, the widespread use of annuities in England constituted a motive for accurate recording.

Odier still felt that it would be unjustifiable to attribute the rise in smallpox deaths to the practice of inoculation, for "if two events happen at the same time or in immediate succession, it does not follow that one is the cause of the other." There were many other aspects to be considered before a decision could be reached.

In his third letter Odier resorted to international comparisons. Geneva had introduced inoculation rather early and had maintained it conscientiously, under high-class medical supervision. A table of Genevan smallpox deaths from 1581 to 1773 showed that during the two decades that had elapsed since the start of inoculation the smallpox mortality had increased. A similar conclusion was reached if the elapsed time was divided into seven-year periods. Odier now wondered whether similar changes had occurred in the death rates from other communicable diseases.

In his fourth letter he considers this question, taking measles as his test-object. If the mortality from measles has undergone the same vicissitudes as smallpox mortality, a common cause may be at work and inoculation can be dismissed from consideration, since measles is not inoculated. The necessary data can be procured only in a city as large as London.

Odier then presents a simple table of deaths from measles in London from 1661 to 1772; the total mortality from all causes is omitted, since it was given in the previous tables. He shows that if the figures for 1661-1716 are compared with those for 1717-1772, whereas smallpox deaths had increased from 62 to 88 per 1,000 nonplague deaths, measles deaths had increased from 6 to 8 per 1000, i.e. in about the same proportion. A table of septennia from 1661 to 1772 shows that, with a few exceptions, deaths from measles tend to rise and fall synchronously with deaths from smallpox.

Measles was chosen for comparison with smallpox because the two diseases were believed to show affinity. Indeed the classical Arab writers considered the two diseases to be the same, except that measles was held to be more "inflammatory" and smallpox more "putrid." Although some agree with this formulation, Odier dissents. His reasons are interesting.

Outbreaks of smallpox and measles, he remarks, tend to be concomitant or immediately successive; this is revealed in the tabulations. John Huxham agreed and suspected that this relation might be indicative of a "diathesis."

But the resemblance between the two diseases must not be allowed to obscure the clinical differences shown by the prodromal symptoms and the eruptions. Moreover, when a person has been attacked by the two diseases simultaneously, the manifestations have tended to remain distinct during the whole course of the illness. Measles usually has tended to retard but not to prevent the eruption of smallpox; the two conditions would not be so distinct if they were the same disease.

Usually each of these two diseases occurs only once in any one person and *never has anyone dreamed of saying that to prevent measles it was sufficient to have had smallpox and vice versa.* If they were the same disease, one would ordinarily take the place of the other.

Cases occur in which smallpox inoculation has communicated mea-

sles, but these are rare. If the two diseases were identical, this would be common.

Whenever smallpox inoculation has caused measles, the inoculation has communicated *both* diseases at the same time. There has been only one case in which an inoculated patient came down with measles without smallpox.

Therefore the two diseases are perfectly distinct and the rise in the mortality from smallpox and measles was due to a common cause; inoculation was not responsible. The cause of the fluctuations in mortality rates is unknown.

COMMENT ON ODIER'S REMARKS

The four letters of Dr. Odier demonstrate clearly the degree of advancement that statistical science had reached since the time of Petty, Graunt, and Halley. This aspect deserves attention.

First, Odier recognizes that his basic data, the London statistics, might harbor a degree of error. He attempted to keep this under at least partial control by using the weekly reports and not the annual compilations, which he considered less reliable. Whether or not this opinion was correct, the attempt to exercise judgment is undeniable. Further, he attempted to purge the original statistics of errors introduced by the inclusion of plague and measles. To reduce the error caused by erroneous reporting, recording, and addition, he resorted to ratios in preference to absolute figures; these ratios were expressed in the old way by means of common fractions but in a few instances were expressed as incidences per 1,000. To sharpen the detection of short-term trends he sometimes divided his series into seven-year or even five-year periods. The importance of large numbers and of long series is recognized by the use of statistics from London. The value of controls is recognized in the comparison between measles and smallpox and in the comparison between Geneva and London.

The incidental effort to clarify the independence of measles as an entity distinct from smallpox is well worth careful perusal. To the old-fashioned clinical reasoning a new element has been added: the knowledge gained by what was in effect a biological experiment—inoculation.

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